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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/936,676	09/14/2001	Christine Libon	PF98PCTSEQ/dln	9130

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EXAMINER	
ZEMAN, ROBERT A	

ART UNIT	PAPER NUMBER
1645	

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04/04/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/936,676	LIBON ET AL.	
	Examiner	Art Unit	
	ROBERT A. ZEMAN	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34,36-38,41-43,49,50 and 55-72* is/are pending in the application.

4a) Of the above claim(s) *36,37 and 55-71* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34,38,41-43,49,50 and 72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10-22-2007 has been entered.

The amendment filed 10-22-2007 is acknowledged. Claims 34, 49 and 72 have been amended. Claim 51 has been canceled. Claims 34, 36-38, 41-43, 49-50 and 55-72 are pending. Claims 36-37 and 55-71 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Claims 34, 38, 41-43, 49-50 and 72 are currently under examination.

Claim Rejections Withdrawn

The rejection of claims 34 and 72 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the term "the Th1 response is close to the Th2 response…" is withdrawn in light of the amendment thereto.

The rejection of claim 49 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the term "carries" is withdrawn in light of the amendment thereto.

The rejection of claims 34, 38 and 72 under 35 U.S.C. 102(b) as being anticipated by Rauly et al. (Research in Immunology, Vol 149 No. 1, page 99, Jan 1998) is withdrawn.

The rejection of claims 34, 38, 41, 43, and 49 under 35 U.S.C. 102(e) as being anticipated by Binz et al. (U.S. Patent 6,197,929) is withdrawn in light of the amendment thereto.

Claim Rejections Maintained

35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

The rejection of claim 72 under 35 U.S.C. 102(e) as being anticipated by Binz et al. (U.S. Patent 6,197,929) is maintained for reasons of record.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37

CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Applicant argues:

1. The instant claims require that the membranes are recovered following a lysing step thereby distinguishing the crude membrane fraction from the purified OmpA protein of described in the art.

2. The membrane fraction of the instant claims is materially distinct from the purified OmpA of Binz et al.

3. The disclosed mixed Th1/Th2 does not meet the limitation of "the Th1 response at least 0.5 times the Th2 response".

Applicant's arguments have been fully considered and deemed non-persuasive.

With regard to Points 1 and 2, Binz et al. disclose a membrane fraction that is recovered from a cell lysate (see Example 1). This fraction is deemed, in absence of evidence to the contrary, to be the same as that of the instant invention.

With regard to Point 3, given that the two compositions are the same they would necessarily possess the same immunological properties.

The instant claims are drawn to methods of inducing a Th1 or mixed Th1/Th2 type response against an antigen utilizing *Klebsiella pneumonia* membrane fractions combined (or covalently bound) with an antigen wherein said antigen if from an infectious agent or is associated with tumor cells. Moreover, said membrane fraction/antigen complexes may be

recombinantly produced, may further comprise peptide/protein that can bind mammalian serum albumin and may be part of pharmaceutical compositions.

Binz et al. disclose the use compositions comprising the outer membrane protein A (OmpA) of *Klebsiella pneumoniae* as an immunopotentiator (carrier/adjuvant). Said protein was recombinantly produced and coupled to protein G of the respiratory syncytial virus (RSV) [see column 3, lines 25-32). Said conjugates may be coupled either covalently or recombinantly [see column 3, lines 9-19] and may further comprise a peptide/protein that can bind mammalian serum albumin [see column 3, lines 20-25] and can be used in pharmaceutical compositions comprising pharmaceutically acceptable excipients [see column 3, lines 49-54]. The disclosed membrane fraction protein:antigen complex (P40-Ext) was disclosed to induce a Th1 response when administered to animals as exemplified by the production of a highly quantitative delayed hypersensitivity response [see column 9, lines 35-41] and macrophage activation [see column 9, lines 50-55].

New Grounds of Rejection

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 34, 38 and 72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rauly et al. (Research in Immunology, Vol 149 No. 1, page 99, Jan 1998).

The instant claims are drawn to methods of inducing mixed Th1/Th2 type response against an antigen utilizing *Klebsiella pneumonia* membrane fractions combined (bound) with an antigen wherein said antigen if from an infectious agent or is associated with tumor cells wherein the Th1 response is "at least 0.5 times" the Th2 response. Moreover, said membrane fraction/antigen complexes may be recombinantly produced and may be part of pharmaceutical compositions.

Rauly et al. disclose the use compositions comprising the outer membrane protein A (OmpA) of *Klebsiella pneumoniae* as an immunopotentiator (carrier/adjuvant). Said protein was recombinantly produced and coupled to a B-cell epitope derived from the respiratory syncytial virus. The resulting complex (rP40-G1) induces a mixed Th1/Th2 response when administered to animals.

Rauly et al. differs from the instant invention in that the OmpA was produced recombinantly. However, given that the OmpA of Rauly et al. is a normal component of *Klebsiella pneumonia* membranes it would have been obvious for the skilled artisan to utilize *Klebsiella pneumonia* membrane fractions in order to take advantage of the reduced preparation costs.

One would have had a reasonable expectation of success given that Rauly et al. disclose Klebsiella *pneumonia* OmpA possesses the claimed immunological properties.

Regarding the limitation that the Th1 response be at least 0.5 times the Th2 response, it is deemed that given that the two compositions are the same they would necessarily possess the same immunological properties.

Claims 34, 38, 41-43, 49-50 and 72 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Binz et al. (U.S. Patent 6,197,929).

The instant claims are drawn to methods of inducing mixed Th1/Th2 type response against an antigen utilizing *Klebsiella pneumonia* membrane fractions combined (bound) with an antigen wherein said antigen if from an infectious agent or is associated with tumor cells wherein the Th1 response is "at least 0.5 times" the Th2 response. Moreover, said membrane fraction/antigen complexes may be recombinantly produced and may be part of pharmaceutical compositions.

Binz et al. disclose the use compositions comprising the outer membrane protein A (OmpA) of *Klebsiella pneumoniae* as an immunopotentiator (carrier/adjuvant). Moreover, Binz

discloses a method of isolating and purifying membrane fractions (see Example 1). Binz et al. additionally disclose that said protein was recombinantly produced and coupled to protein G of the respiratory syncytial virus (RSV) [see column 3, lines 25-32). Said conjugates may be coupled either covalently or recombinantly [see column 3, lines 9-19] and may further comprise a peptide/protein that can bind mammalian serum albumin [see column 3, lines 20-25] and can be used in pharmaceutical compositions comprising pharmaceutically acceptable excipients [see column 3, lines 49-54]. The disclosed membrane fraction protein:antigen complex (P40-Ext) was disclosed to induce a Th1 response when administered to animals as exemplified by the production of a highly quantitative delayed hypersensitivity response [see column 9, lines 35-41] and macrophage activation [see column 9, lines 50-55].

Binz et al. differs from the instant invention in that they don't explicitly disclose the use of all the membrane fractions as an immumodulator. However, given that the OmpA of Binz et al. is a normal component of *Klebsiella pneumonia* membranes it would have been obvious for the skilled artisan to utilize any or all of the *Klebsiella pneumonia* membrane fractions obtained by the method set forth in Example 1, in order to take advantage of the reduced preparation costs.

One would have had a reasonable expectation of success given that Binz et al. disclose a *Klebsiella pneumonia* OmpA that possesses the claimed immunological properties.

Regarding the limitation that the Th1 response be at least 0.5 times the Th2 response, it is deemed that given that the two compositions are the same they would necessarily possess the same immunological properties.

35 USC § 112, New Matter

Claims 34, 38, 41-43, 49-50 and 72 are is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicant has amended the claims 34 and 72 to recite "the Th1 response is at least 0.5 times the Th2 response…" This phrase does not appear in the specification, or original claims as filed. The portion of the specification relied on for support by Applicant deals only with the ratio of IgG2a antibodies and IgG1 antibodies directed to the same antigen but does not address any other measure of Th1 and Th2 immune responses. Therefore this limitation is new matter.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT A. ZEMAN whose telephone number is (571)272-0866. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on (571) 272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov.

Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert A. Zeman/
Primary Examiner, Art Unit 1645
March 27, 2008